REVIEW ARTICLE

# Monkeypox Disease and Vaccine: A Comprehensive

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## ABSTRACT

While the world was still recovering from horrors of the Coronavirus disease 2019 (COVID-19), another viral disease, this time the Monkeypox virus, a member of Orthopoxvirus genus[1] of the Poxviridae family started spreading. Monkeypox is a zoonotic infection with rare instances of human-to-human transmission reported worldwide[2].Monkeypox gets its name from the Macaque monkeys in whom this viral infection was first witnessed[3]. Owing to an outbreak in 2022, Monkeypox virus disease which was previously known to be endemic to certain regions of Africa was reported from regions of Europe and western hemisphere[4]. Extensive research and advent of vaccines have been the front- runners in containing the outbreak.

## INTRODUCTION

Monkeypox disease is an infectious zoonotic disease caused by Monkeypox virus, a member of Poxviridaefamily[1,2]. It belongs to genus Orthopoxvirus, same as that of Smallpox, Cowpox and Vaccinia virus[5]. Like the other members of Poxviridae family,Monkeypox viruses also are large, enveloped, linear double stranded DNA viruses with a genome size ranging from 130-360kbp[6]. Several animal species are known to be susceptible to the Monkeypox virus like squirrels, Gambian pouched rats, dormice, and non-human primates[2].

Monkeypox virus was first observed in laboratory monkeys in Copenhagen, Denmark in 1958[7]. However the first human case was not reported till 1970 when a 9-month-old boy was found positive for the virus during mass screening for the Smallpox virus in Zaire (now known as Democratic Republic of Congo)[8].

The first case of the recent outbreak of Monkeypox disease was reported on May 6, 2022 in United Kingdom. The outbreak spread out from Central and West Africa to other continents[9]. On July 23, 2022, WHO declared the outbreak a public health emergency of international concern (PHEIC)[10]. As of September 30, 2022, 12 cases of Monkeypox disease have been reported in India in addition to 68,428 confirmed cases in 106 countries worldwide[9].

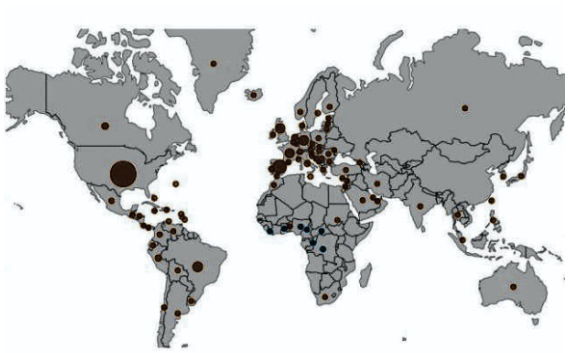

**Fig 1: Worldwide distribution of Monkeypox**

Photo Credit: /www.cdc.gov/poxvirus/monkeypox/response/2022/world-map

### Epidemiology:

Monkeypox disease is originally known to be endemic to Sub-Saharan Africa for hundreds of years with thousands of cases reported annually. The disease became a matter of global concern for public health in 2003, when an outbreak was reported in United States of America linked to infective pet dogs[11]. The natural host and the reservoir of the Monkeypox virus still remains a mystery with studies suggesting both humans and monkeys as incidental hosts.

The Monkeypox virus is known to have two clades: West Africa(WA) clade and the Congo Basin(CB) clade with the latter known to be more virulent. However

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in the current outbreak , West African clade seems to be responsible for the sudden rise of cases in Europe and other parts of the world[12]. Epidemiological studies suggest an $R_0$ value (degree of transmissibility of disease) ranging from 1.10 to 2.40 for the disease with case fatality rate estimated at 0-3% for West African clade and 0-11% for Congo Basin clade[11].

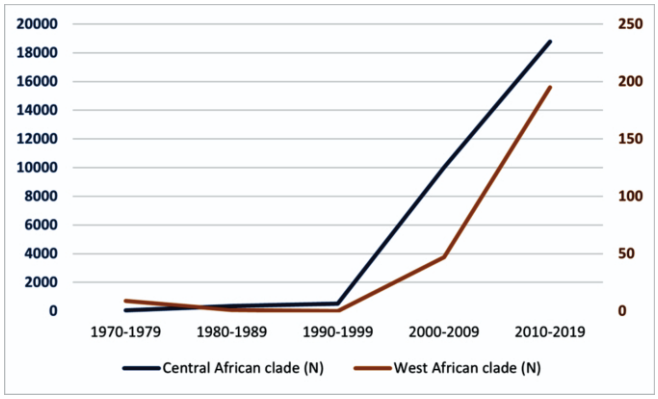


**Fig 1: Case distribution of the two clades over the years.**

Photo Credit: **The changing epidemiology of human monkeypox—A potential threat? A systematicreview**

**Transmission and Pathogenesis:**

Monkeypox virus primarily infects invertebrates and lower mammals. Animal-to-human transmission is the chief reason for presence of disease in humans. Animal-to-human transmission can result either from direct contact with blood and body fluids or from cutaneous and mucosal lesions of infected animals[13]. Human-to-human transmission can occur from close contact with respiratory secretions, or skin lesions of an infected person. Transplacental transmission from mother to fetus is also a possibility and may give rise to Congenital Monkeypox disease. Few cases of perinatal transmission have also been reported. The sexual route of transmission is still under evaluation with early reports from certain studies suggesting higher prevalence in men who have sexual contact with other men[11].

The incubation period for the disease ranges from 5-21 days with person being non-contagious throughout this period implying that infection is spread only after symptoms appear. The virus multiplies at the site of inoculation before entering the blood stream. Lesions appear 2-3 days after onset of fever and are mainly maculo-papular in nature. Serum antibodies also become positive by this period[14].

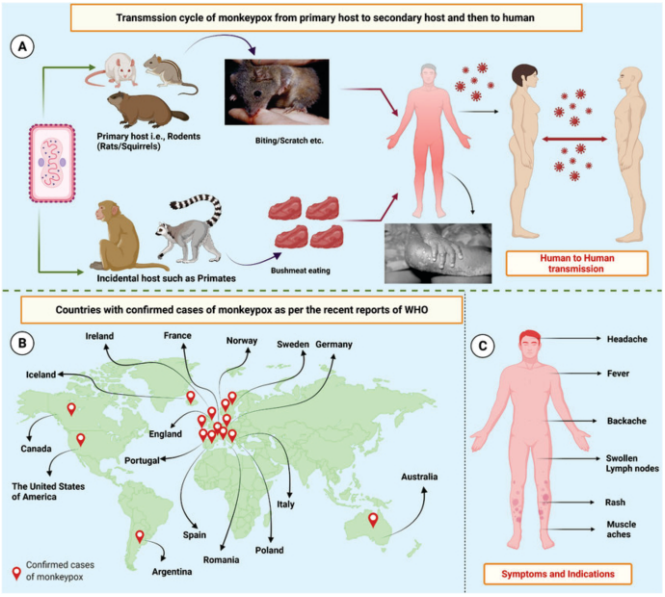


**Fig 2: Guide Map to Monkeypox disease**

**Photo Credit:** Emergence of monkeypox: Risk assessment and containment measures ;**June 2022; O.P.Chaudhary et al.**

**Clinical Features:**

Monkeypox is usually a self-limiting disease with symptoms lasting from 2 to 4 weeks. Severe cases occur more commonly among children and are related to the extent of virus exposure, patient health status and nature of complications. Underlying immune deficiencies like diabetes mellitus and AIDS may lead to more detrimentaloutcomes[14].

The initial five days called invasion period manifests with fever, headache, lymphadenopathy, back pain, myalgia and asthenia. Lymphadenopathy is a typical feature of monkeypox distinguishing it from the early stages of similar diseases like chickenpox, measles and smallpox[11,13].

The skin eruption commonly appears within 1-3 days after the onset of the fever. The rash appears predominantly on the face and extremities sparing the trunk. Lesions can also be seen on the oral mucosa, genitalia, conjunctiva as well as the cornea[14].

The rash evolves in textbook fashion from flat base to macules to papules to vesicles to pustules and crusts which in due course eventually dry up and fall off.

**Fig 3: Examples of Monkeypox disease Rashes**
Photo credit: UK Health Security Agency

**Complications:**

Complications of Monkeypox disease include secondary infections, bronchopneumonia, sepsis, encephalitis, and infection of the cornea with ensuing loss of vision. However the extent to which the asymptomatic infection may occur remainsunknown[15].

**Lab Diagnosis and Differential Diagnosis:**

Polymerase Chain Reaction (PCR) remains the diagnostic modality of choice for the disease. Samples are taken from active skin lesions. PCR is believed to have higher sensitivity even in presence of bacterial contamination[11].A hybridization assay, utilizing probe(MGB Eclipsetrade mark probe), targets envelope protein gene (B6R) and specifically detects Monkeypox virus (MPXV)[16].

Diseases like chickenpox, measles, bacterial skin infections, scabies, syphilis and medication-associated allergies which manifest with rashes serve as important differential diagnoses for the Monkeypox virus disease owing to the presence of classical rashes in the Monkeypox disease too. However the typical rash pattern and presence of lymphadenopathy in prodromal stages of the illness are the characteristic features of the Monkeypox disease[14].

**Treatment:**

The management of Monkeypox disease is primarily based on providing symptomatic relief and at the same time preventing potentially fatal complications. DNA Polymerase inhibitors like Cidofovir known to be effective in animals are under trial for human use in Monkeypox disease[11]. Recently, a drug Tecovirimat which inhibits **p37**, a highly conserved protein in all orthopoxviruses known to mediate the formation of enveloped virions, has been approved for use against Monkeypox disease in various countries[11,14,17].

United States Food and Drug Administration has also licensed Vaccinia Immunoglobulins (known to be effective against Orthopoxviruses) for effective management and adequate prophylaxis against the fast spreading disease[11].

**Vaccines and Vaccination:**

Vaccines against Smallpox disease have been demonstrated to be about 85% effective in preventing Monkeypox disease. A still newer vaccine based on a modified, attenuated, Vaccinia virus strain (Ankara strain) was approved for the prevention of Monkeypox in 2019. This vaccine is a third generation smallpox virus and is given in two-doses for which availability remains limited[18,19]. Live attenuated, non-replicating smallpox and Monkeypox vaccine that elicits both humoral and cellular immune response to orthopoxviruses is under clinical trials.

Vaccination is indicated for the prevention of Monkeypox disease in adults who are at high risk of contracting the infection. It has been 40 or more years since all countries stopped routine smallpox vaccination with vaccinia-based vaccines that protected against Monkeypox. The population unvaccinated against small poxwhich is born after 1980 is more susceptible to Monkeypox virus infection.

**Dosing:**

a) Subcutaneous Administration: 0.5 mL SC x2 doses; 4 weeks apart
b) Intradermal Administration: 0.1 mL ID x2 doses; 4 weeks apart (Emergency Use Authorization) [18]

**Adverse Effects:**

Local side effects include injection site pain, redness, swelling, induration and itching. Systemic manifestations include muscle pain, headache, fatigue, nausea and chills.

**Pregnancy:**

Human data are insufficient to inform vaccine-associated risks in pregnancy.Studies in animals revealed no evidence of harm to the fetus.

**Lactation:**

Unknown if excreted in human milk; data are not available to assess vaccine effects in breastfed infants or on milk production/excretion[18,19,20].

**Prevention:**

Forewarned is forearmed therefore educating people about risk factors and mitigating the exposure to the virus to minimum are chief strategies for prevention. Due to reported human-to-human transmission by respiratory secretions, isolation of the diseased and Quarantine of those exposed also seems as a strong strategy.

The Ministry of Health and Family Welfare (MoHFW), Government of India has already released guidelines on the detection and management of Monkeypox disease. The National Institute of Virology (NIV) in Pune has been designated as nodal laboratory for Monkeypox virus testing in India[11].

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